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(54) [Title of the Invention] An Adrenocortical Hormone Secretion Inhibitory Agent

(57) [Abstract]

[Structure] An adrenocortical hormone secretion inhibitory agent comprised of essence of plants of the family Labiatae and compositions of cosmetics, medicinal drug products and food products that contain them.

[Effect] Because excess secretion of adrenocortical hormone is inhibited by means of this invention, vascular impairment caused by it is prevented.

[Claims]

[Claim 1]
An adrenocortical hormone secretion inhibitory agent comprised of essence of plants of the genus Labiatae.

[Claim 2] An adrenocortical hormone secretion inhibitory agent as described in Claim 1 in which the plant of the family Labiatae may be lavender, marjoram, thyme, sage, basil, peppermint, spearmint, rosemary, catnip, lemon palm, oregano, Japanese mint and beefsteak plant.

[Claim 3] An adrenocortical hormone secretion inhibitory agent as described in Claims 1 or 2 in which the essence is a component in the plant body having a melting point less than 200°C.

[Claim 4] An adrenocortical hormone secretion inhibitory agent as described in any one of Claims 1 to 3 in which the adrenocortical hormone is cortisol.

[Claim 5] An adrenocortical hormone secretion inhibitory agent as described in any one of Claims 1 to 4 in which the secretion of the adrenocortical hormone is by way of secretion in saliva.

[Claim 6] A stress relaxant that is comprised of the adrenocortical hormone secretion inhibitory agent described in any one of Claims 1 to 5.

[Claim 7] A composition that contains one or two or more substances selected from the stress relaxant described in Claim 6.

[Claim 8] A composition that contains the adrenocortical hormone inhibitory agent described in any one of Claims 1 to 5.

[Detailed Description of the Invention]

[0001]

[Technological field of the invention] This invention relates to an adrenocortical hormone secretion inhibitory agent, a stress relaxant and a composition that contains them.

[0002]

[Prior art] No one can deny that the present time is an age of stress and those that live in modern societies live lives in which they are subjected to excessive stress. For this reason, the typical diseases of modern people are psychosomatic conditions such as anorexia, insomnia, hyperphagia, neurosis and refusal to go to work. Although karaoke and so-called nominication [TRANSLATOR's NOTE: This appears to be a made-up word based on the word "communication" using 'nomi" = drinking, instead of "commu" =; a good equivalent might be "communal drinking"] is widely practiced in order to reduce these stresses, it goes without saying that these measures are not healthy. Sports are also a means for dissipating stress. However, moderate participation in sports when one is very busy is either of little effect or presents a considerable danger of bringing on a heart attack. From this standpoint, a means for reducing stress without being immoderate is sought.

[0003] There are two types of adrenocortical hormones, glucocorticoids and mineralocorticoids and they are said to play various roles. For example, glucocorticoids promote sugar production in the liver, elevating blood sugar levels. In muscle, they promote breakdown of protein, and, in adipose tissue, they promote breakdown of fat, increasing the quantity of free fatty acids in the blood. In addition, they inhibit edema, capillary dilation, fibrin deposition, neutrophil migration, phagocytic action, proliferation of fibroblasts and granulation due to inflammation. Mineralocorticoids act on the distal urinary tubules of the kidneys, promoting reabsorption of sodium and promoting urinary excretion of potassium and

hydrogen ions. Of the two, it is said that glucocorticoids are substances that are highly involved in stress and it is said that the quantity of secretion of glucocorticoids into the blood is increased when stress is strongly felt. However, it is not known what effect the presence of senna fragrance has on body fluid concentrations of glucocorticoids in states of high stress.

[0004] Although it is said that fragrances, of which senna is representative, have an anti-stress effect, no instances are known in which such an effect has actually been confirmed. In addition, there has been no quantification of the positive stress effects of senna. Moreover, it is not known whether senna has the anti-stress action or the superior glucocorticoid decreasing action of plants of the family Labiatae.

[0005]

[Problems the invention is intended to solve] This invention was developed under these circumstances and has the objective of providing an adrenocortical hormone secretion inhibitory agent which inhibits the secretion of adrenocortical hormones, which is a convenient index of stress, and which lowers the concentration of adrenocortical hormone in body fluids.

[0006]

[Means for solving the problems]. In the light of these circumstances, the inventors conducted repeated screening studies of various raw materials in order to find an adrenocortical hormone secretion inhibitory agent which inhibits the secretion of adrenocortical hormones, which is a convenient index of stress, and which lowers the concentration of adrenocortical hormone in body fluids. As a result, they perfected this invention by discovering such an action in essence of plants of the family Labiatae.

(0007) (1) Adrenocortical hormone secretion inhibitory agents of this invention

The adrenocortical hormone secretion inhibitory agents of this invention are comprised of essence of plants of the family Labiatae. Plants of the family Labiatae include, for example, lavender, marjoram, thyme, sage, basil, peppermint, spearmint, rosemary, catnip, lemon palm, oregano, Japanese mint and beefsteak plant. It can be anticipated that any of them have an adrenocortical hormone secretion inhibitory action. Of these, lavender, marjoram, mint and basil are preferable, and, among the latter, lavender, mint and basil are particularly desirable. The term essence that is referred to in this invention is a general term referring to processed products that are obtained by drying, finely cutting and pulverizing the bodies of these plants, extracts obtained by extracting the plant body or processed product thereof with a solvent and removing the solvent from the extracted material, distilled products obtained by distillation or steam distillation of plant bodies or processed products thereof and refined products obtained by subjecting extracts or distilled substances to column chromatography or solution extraction. Here, steam distillation may be performed in the usual way by blowing steam at the plant body or processed product thereof, cooling the matter that is distilled out and separating it into the aqueous phase and the organic phase and collecting the organic phase. Extraction may be performed over a period of several days when the solvent is added to the plant body or processed product thereof in an amount of 0.5 to 10 times its volume and the materials are at room temperature or may be performed by immersion for several hours when the temperature is close to the boiling point. Solvents that can be cited include, for example, alcohols such as methanol and ethanol, esters such as ethyl acetate and methyl acetate, nitriles such as acetonitrile, ethers such as diethyl ether and tetrahydrofuran, halogenated hydrocarbons such as chloroform and methylene chloride and ketones such as acetone and methyl ethyl ketone. Any of these substances can be used in this invention. However, of these, among the plant structural components obtained by distillation, low boiling point components, i.e., components with boiling points less than 200°C, are preferable. The reason for this is that a safe adrenocortical hormone secretion inhibitory action can be anticipated m st effectively in cases in which the adrenocortical hormone secretion inhibitory agent of this invention is stimulated through the sense of smell by means of fragrances. The adrenocortical hormone secretion inhibitory agent of this invention, as shown in the examples to be described subsequently, has the action of lowering the concentration of the adrenocortical hormones in the saliva through the agency of the sense of smell.

[0008] (2) Relationship between stress load and adrenocortical hormones

Although there is a deep relationship between stress and adrenocortical hormones, and, especially, with glucocorticoids, there are no examples in which these relationships have actually been confirmed. Using cortisol as the glucocorticoid, the following experiment was performed in order to ascertain the relationship between stress load and cortisol. Specifically, twenty test subjects were assembled, calculations of mathematical operations were performed to two places for 30 minutes with a delay of 4 seconds per problem. Saliva was collected 30 minutes before and after and the cortisol concentration in the saliva was found by radioimmunoassay, which indicates the state of execution of this invention to be described subsequently. The percentage of cortisol added to the saliva was found by the following calculation: (concentration of cortisol after calculation – concentration of cortisol before calculation)/(concentration of cortisol before calculation) * 100. Similarly, these values were found on other days when the delay time was set to 3 seconds and when the time for solving the problem was set to 40 minutes. The results are shown in Table 1. From this table, it can be seen that the percentage of cortisol added increased proportionally to the amount of cortisol load. Specifically, it was found that the amount of secretion of glucocorticoid, of which cortisol is representative, into the saliva can serve as an index of the intensity of stress. That is, it can be said that a substance that decreases the amount of secretion of glucocorticoid of which cortisol is representative is a substance that can reduce stress.

[0009]

[Table 1]

Conditions	Average percentage of cortisol added (%)
Delay of 4 seconds; 30 minutes	43
Delay of 3 seconds; 30 minutes	62
Delay of 4 seconds; 40 minutes	56

[0010] (3) Action of the adrenocortical hormone secretion inhibitory agent of this invention

The adrenocortical hormone secretion inhibitory agent of this invention has the action of relaxing stress by means of stimulating the sense of smell as a fragrance. As a result, it has the actions of inhibiting the secretion of adrenocortical hormone in saliva and lowering its concentration. The adrenocortical hormone secretion inhibitory agent of this invention acts as a fragrance. The use amount at which this effect is manifested is 0.01 to 10 mg/m^3. This is desirable because the sense of smell is stimulated at this concentration. The source plants of this invention are all widely used as foods so that there is no worry about them displaying toxicity at these concentrations.

[0011] (4) The composition of this invention

The composition of this invention is characterized in that it contains the adrenocortical hormone secretion inhibitory agent described above. There are no particular limitations on the type of composition as long as the stimulation by the adrenocortical hormone secretion inhibitory agent of this invention is transmitted via the sense of smell. For example, it may be in the form of a fragrant product such as potpourri, a room fragrance, perfume or toilet water, a food product such as gum or candy or a

beverage such as juice or cold drinks. Any desired component that is ordinarily used in such compositions can be used in the composition of this invention in addition to the adrenocortical hormone secretion inhibitory agent. Such components in fragrant products can include, for example, hydrocarbons such as vaseline and microcrystalline waxes, esters such as jojoba oil and spermaceti, triglycerides such as tallow and olive oil, higher alcohols such as cetanol and oleyl alcohol, fatty acids such as stearic acid and oleic acid, polyvalent alcohols such as glycerol and 1,3-butanediol, nonionic surfactants, anionic surfactants, cationic surfactants, amphoteric surfactants, thickeners such as ethanol and carbobol [sic], preservatives, ultraviolet ray absorbents, antioxidants, pigments and powders. In food products and beverages, they can include flavor and odor enhancing agents, sweeteners, acid flavoring agents, oils and fats, thickeners, emulsion stabilizers, water, carbonic acid, excipients and binders. The desirable content of the adrenocortical hormone secretion inhibitory agent of this invention in these compositions in fragrant products is 0.01 to 60 weight %, more preferably, 0.05 to 40 weight %, and, most preferably, 0.1 to 30 weight %. In food products or beverages, it is 0.01 to 30 weight %, more preferably, 0.05 to 20 weight %, and, most preferably, 0.01 to 10 weight %. These compositions can be manufactured by any known method.

[0012]

[Mode of execution of the invention] We shall now present a detailed description of the mode of execution of this invention by presenting examples. However, it goes without saying that this invention is not limited solely to these examples.

[0013] Example 1 (Example of Manufacture)

1 kg of whole dried leaves of lavender was pulverized and subjected to steam distillation. The matter insoluble in water was collected and 0.7 g of adrenocortical hormone secretion inhibitory agent 1 was obtained.

[0014] Example 2 (Example of Manufacture)

1 kg of dried leaves of peppermint was pulverized and subjected to steam distillation. The matter insoluble in water was collected and 1.1 g of adrenocortical hormone secretion inhibitory agent 2 was obtained.

[0015] Example 3 (Example of Manufacture)

1 kg of dried leaves of spearmint was pulverized and subjected to steam distillation. The matter insoluble in water was collected and 0.8 g of adrenocortical hormone secretion inhibitory agent 3 was btained.

[0016] Example 4 (Example of Manufacture)

1 kg of dried leaves of marjoram was pulverized and subjected to steam distillation. The matter insoluble in water was collected and 0.7 g of adrenocortical hormone secretion inhibitory agent 4 was obtained.

[0017] Example 5 (Example of Manufacture)

1 kg of dried leaves of basil was pulverized and subjected to steam distillation. The matter insoluble in water was collected and 1.2 g of adrenocortical hormone secretion inhibitory agent 5 was obtained.

[0018] Example 6 (Example of Manufacture)

1 kg of dried leaves of lemon palm was pulverized and subjected to steam distillation. The matter insoluble in water was collected and 0.9 g of adrenocortical hormone secretion inhibitory agent 6 was obtained.

[0019] Example 7 (Example of Manufacture)

1 kg of dried leaves of sage was pulverized and subjected to steam distillation. The matter insoluble in water was collected and 0.8 g of adrenocortical hormone secretion inhibitory agent 7 was obtained.

[0020] Example 8 (Example of Manufacture)

1 kg of dried leaves of rosemary was pulverized and subjected to steam distillation. The matter insoluble in water was collected and 1.3 g of adrenocortical hormone secretion inhibitory agent 8 was obtained.

[0021] Example 9 (Example of Manufacture)

1 kg of dried leaves of catnip was pulverized and subjected to steam distillation. The matter insoluble in water was collected and 1.1 g of adrenocortical hormone secretion inhibitory agent 9 was obtained.

[0022] Example 10 (Example of Manufacture)

1 kg of dried leaves of thyme was pulverized and subjected to steam distillation. The matter insoluble in water was collected and 0.6 g of adrenocortical hormone secretion inhibitory agent 10 was obtained.

[0023] Example 11 (Example of Manufacture)

1 kg of dried leaves of oregano was pulverized and subjected to steam distillation. The matter insoluble in water was collected and 0.7 g of adrenocortical hormone secretion inhibitory agent 11 was obtained.

[0024] Example 12 (Example of Manufacture)

1 kg of dried leaves of beafsteak plant was pulverized and subjected to reflux for 2 hours in 3 liters of methanol. Extraction was then performed, the solvent was removed and 2.1 g of adrenocortical hormone secretion inhibitory agent 12 was obtained.

[0025] Example 13 (Example of Manufacture)

1 kg of dried leaves of Japanese mint was pulverized and subjected to reflux for 2 hours in 5 liters of methanol. Extraction was then performed, the solvent was removed and 2.5 g of adrenocortical hormone secretion inhibitory agent 13 was obtained.

[0026] Examples 14 to 20 (Compounding Examples)

Room fragrances were manufactured in accordance with the formulations shown in Table 2. Specifically, the formulation components were heated and dissolved and were poured into containers in which they were allowed to harden, with room fragrances being obtained.

[0027]

[Table 2]

Component	Example 14	Example 15	Example 16	Example 17	Example 18	Example 19	Example 20
Carnauba wax	60	50	50	50	50	50	50
Liquid paraffin	30	30	30	30	30	30	30
Example 1	10						
Example 2		10					
Example 3			10				
Example 4				10			
Example 5					10		
Example 6						10	
Example 7							10

[0028] Examples 21 to 27 (Compounding Examples)

Calm [phonetic]* fragrances were manufactured in accordance with the formulations shown in Table 3. Specifically, the formulation components were heated and dissolved, packed in containers and wicks were installed, with calm [phonetic] fragrances being obtained.

[0029]

[Table 3]

Component	Example 21	Example 22	Example 23	Example 24	Example 25	Example 26	Example 27
Ethanol	50	50	50	50	50	50	50
PEG 400	30	30	30	30	30	30	30
Example 8	10						2
Example 9		10					2
Example 10			10				2
Example 11				10			2
Example 12					10		1
Example 13						10	1

[0030] Examples 28 to 34

Toilet water was made in accordance with the formulations shown in Table 4. Specifically, the formulation components were heated and stirred at 80° and solubilized, with toilet water being obtained.

* [Translator's Note: Transliterated phonetically from the Japanese. As such, the spelling may differ from other transliterations.]

[0031]

[Table 4]

Component	Example 28	Example 29	Example 30	Example 31	Example 32	Example 33	Example 34
Ethanol	10	10	10	10	10	10	10
Propanol	6	5	5	5	5	5	5
Methylparaben	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Tincture	82.9	82.9	82.9	82.9	82.9	82.9	82.0
Example 1	1						
Example 2		1					
Example 3			1				
Example 4				1			
Example 5					1		
Example 6						1	
Example 7							1

[0032] Examples 35 to 41 (Compounding Examples)

Hair tonics were prepared in accordance with the formulations shown in Table 5. Specifically, the formulation components were weighed out, stirred and solubilized, with hair tonics being obtained.

[Table 5]

Component	Example 35	Example 36	Example 37	Example 38	Example 39	Example40	Example 41
Ethanol	50	50	50	50	50	50	50
Propanol	5	5	5	5	5	5	5
Cayenne pepper	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Tincture	42.9	42.9	42.9	42.9	42.9	42.9	42.0
Example 8	1						0.2
Example 9		1					0.2
Example 10			1				0.2
Example 11				1			0.2
Example 12					1		0.1
Example 13						1	0.1

[0033] Examples 42 to 48 (Compounding Examples)

Candy was made in accordance with the formulations shown in Table 6. Specifically, the formulation components were heated at 120°C and made to a uniform state. They were then molded and candy was obtained.

[0034]

[Table 6]

Component	Example 42	Example 43	Example 44	Example 45	Example 46	Example 47	Example 48
White sugar	50	50	50	50	50	50	50
Thick malt syrup[**]	30	30	30	30	30	30	30
Citric acid	5	5	5	5	5	5	5
Example 1	15						
Example 2		15					
Example 3			15				
Example 4				15			
Example 5					15		
Example 6						15	
Example 7							15

**[Translator's Note: The Japanese characters are very poorly legible]

[0035]

[Example]

Example 1

A study was conducted of the adrenocortical hormone secretion inhibitory action of adrenocortical hormone secretion inhibitory agents 1 to 13 of Examples 1 to 13. The 30-minute calculation load procedure with a delay of 4 seconds described above was performed using 20 test subjects in the presence of adrenocortical hormone secretion inhibitory agents 1 to 13. In the control group, it was performed in the absence of a fragrance. Saliva was collected before and after the procedure and quantitative determinations of cortisol were performed using gamma cortocortisol [TRANSLATOR's NOTE: This appears to be a typographical error for "gamma counter"]. Specifically, the saliva was frozen for 24 hours at -20°C and then restored to 5°C. It was then centrifuged for 15 minutes at 3000 cpm and the supernatant was collected. One vial of the tracer solution of the kit was thoroughly mixed with 100 ml of the buffer solution of the kit to make a tracer buffer solution. The antibody tubes of the kit were used respectively as the test sample and a blank and 200 μl of physiological saline solution and standard solution of cortisol were introduced. Amounts of 1 ml of tracer buffer solution were added to these tubes. Amounts of 1 ml of tracer buffer solution were added to the tubes (T1, T2) for total count determination, caps were placed on them and they were used as total count tubes. These tubes were incubated for 45 minutes at 37°C. The content solution was removed, and determinations were made of the total radioactivity of the tubes with a gamma counter. Radioactivity relative to the standard solution was plotted, a calibration curve was prepared and the concentrations of cortisol in each test sample were calculated from this calibration curve. As comparison products, leaf alcohols, which are fragrant components of forests, and linalool, which is a fragrant component of citrus fruits, were used. The results are shown in Table 7. The unit of the numerical values in the table is μg/dl. From this table, it can be seen that the adrenocortical hormone secretion inhibitory agent of this invention significantly decreased the concentration f cortisol in saliva. Further, the amount of decrease was higher than that leaf alcohols and linalool. It is also clear from the experimental results that the anti-stress effects of senna were evaluated quantitatively.

[0036]

[Table 7]

Test sample	Before the procedure	After the procedure
Cortisol	0.240	0.351
Adrenocortical hormone secretion inhibitory agent 1	0.247	0.312
Adrenocortical hormone secretion inhibitory agent 2	0.248	0.299
Adrenocortical hormone secretion inhibitory agent 3	0.250	0.284
Adrenocortical hormone secretion inhibitory agent 4	0.239	0.287
Adrenocortical hormone secretion inhibitory agent 5	0.251	0.331
Adrenocortical hormone secretion inhibitory agent 6	0.246	0.319
Adrenocortical hormone secretion inhibitory agent 7	0.255	0.335
Adrenocortical hormone secretion inhibitory agent 8	0.241	0.322
Adrenocortical hormone secretion inhibitory agent 9	0.249	0.329
Adrenocortical hormone secretion inhibitory agent 10	0.253	0.341
Adrenocortical hormone secretion inhibitory agent 11	0.235	0.333
Adrenocortical hormone secretion inhibitory agent 12	0.245	0.328
Adrenocortical hormone secretion inhibitory agent 13	0.255	0.330
Leaf alcohol	0.256	0.345
Linolool	0.240	0.339

[0037]

[Effect of the invention] By means of this invention, secretion of adrenocortical hormone, which is a convenient index of stress, can be inhibited and the concentration of adrenocortical hormone in saliva can be decreased.

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(54)【発明の名称】　副腎皮質ホルモン分泌抑制剤

(57)【要約】

【構成】　シソ科植物のエッセンスからなる副腎皮質ホルモン分泌抑制剤及びそれを含有する化粧料、医薬品、食品などの組成物。

【効果】　本発明によれば、副腎皮質ホルモンの過剰な分泌が抑制できるので、これに起因する血管系障害などが防げる。。

【特許請求の範囲】
【請求項１】　シソ科植物のエッセンスからなる副腎皮質ホルモン分泌抑制剤。
【請求項２】　シソ科植物が、ラベンダー、マージョラム、タイム、セイジ、バジル、ペパーミント、スペアミント、ローズマリー、キャットニップ、レモンバーム、オレガノ、ニホンハッカ、シソの何れかである、請求項１記載の副腎皮質ホルモン分泌抑制剤。
【請求項３】　エッセンスが植物体中の沸点２００℃未満の成分である、請求項１又は２記載の副腎皮質ホルモン分泌抑制剤。
【請求項４】　副腎皮質ホルモンがコルチゾールである、請求項１～３の何れか一項に記載の副腎皮質ホルモン分泌抑制剤。
【請求項５】　副腎皮質ホルモンの分泌が唾液中への分泌である、請求項１～４の何れか一項に記載の副腎皮質分泌抑制剤。
【請求項６】　請求項１～５の何れか一項に記載の副腎皮質ホルモン分泌抑制剤からなる、ストレス緩和剤。
【請求項７】　請求項６記載のストレス緩和剤から選ばれる１種乃至は２種以上を含有する組成物。
【請求項８】　請求項１～５の何れか一項に記載の副腎皮質ホルモン分泌抑制剤を含有する組成物。
【発明の詳細な説明】
【０００１】
【発明の属する技術分野】本発明は、副腎皮質ホルモン分泌抑制剤、ストレス緩和剤及びそれらを含有する組成物に関する。
【０００２】
【従来の技術】現在はストレスの時代であり、現代社会に生きる者が過剰のストレスを受けて生活していることを否定する者はいない。この為、現代人の典型的な疾病に、拒食症、不眠症、過食症、ノイローゼ、出社拒否症等の心身症がある。これに対してこの様なストレスを軽減するため、広くカラオケやいわゆるノミニケーションが行われているが、この様な対処が健全でないことは言うまでもない。ストレスを発散する手段としてスポーツがあるが、多忙な中で無理に行うスポーツは効果が少ないばかりか、心臓発作を招くなど危険な面が少なくない。この様な観点に於いて、無理無くストレスを緩和する手段が求められていた。
【０００３】又、一方、副腎皮質ホルモンには、糖質コルチコイドと鉱質コルチコイドの２種が存在し、これらには種々の役割があるといわれている。例えば、糖質コルチコイドは肝臓での糖新生が促進され血糖を上昇させたり、筋肉ではタンパク質の分解を促進したり、脂肪組織では脂肪分解を促進し血中遊離脂肪酸量を増加させる。又、炎症による浮腫、毛細血管拡張、フィブリン沈着、好中球遊走、喰作用、線維芽細胞増殖、肉芽形成等が抑制するし、鉱質コルチコイドは腎遠位尿細管に作用し、ナトリウムの再吸収を促進し、カリウム、水素イオンの尿中排泄を促進する。このうち、糖質コルチコイドはストレスと深く係わっている物質といわれており、ストレスを強く感じるとき血中へのこの糖質コルチコイドの分泌量が増加すると言われている。しかし、ストレス負荷状態に於いて、ハーブの香りの存在がどの様に糖質コルチコイドの体液濃度に影響を与えるかは知られていない。
【０００４】更に、ハーブに代表される香料などの効果として抗ストレス効果があることは言われているが、その効果を実際に確かめた例は知られていない。又、ハーブの好ストレス効果を定量化することは行われていない。更に、ハーブの内、シソ科の植物が抗ストレス作用或いは糖質コルチコイド低下作用に優れていることも知られていない。
【０００５】
【発明が解決しようする課題】本発明はこの様な状況下行われたものであり、手軽にストレスの指標である、副腎皮質ホルモンの分泌を抑制し、体液中の副腎皮質ホルモンの濃度を低下させる副腎皮質ホルモン分泌抑制剤を提供することを課題とする。
【０００６】
【課題を解決するための手段】本発明者等はこの様な状況に鑑みて、手軽にストレスの指標である、副腎皮質ホルモンの分泌を抑制し、体液中の副腎皮質ホルモンの濃度を低下させる副腎皮質ホルモン分泌抑制剤を求めて各種原料を対象にスクリーニング研究を重ねた結果、シソ科植物のエッセンスにその様な作用を見いだし発明を完成させた。以下本発明について詳細に説明する。
【０００７】（１）本発明の副腎皮質ホルモン分泌抑制剤
本発明の副腎皮質ホルモン分泌抑制剤はシソ科植物のエッセンスからなる。シソ科植物としては、例えば、ラベンダー、マージョラム、タイム、セイジ、バジル、ペパーミント、スペアミント、キャットニップ、ローズマリー、レモンバーム、オレガノ、ニホンハッカ、シソ等が例示でき、これらの何れもが副腎皮質ホルモン分泌抑制作用が期待できる。これらの内好ましいものは、ラベンダー、マージョラム、ミント、バジルであり、この中でもラベンダー、マージョラム、ミントが更に好ましい。本発明に言うエッセンスとは、これらの植物の植物体を乾燥、細切、粉砕した加工品、植物体又はその加工品を溶剤で抽出したり、抽出したものから溶剤を除去した抽出物、植物体或いはその加工物を蒸留又は水蒸気蒸留した蒸留物、抽出物或いは蒸留物をカラムクロマトグラフィーや液液抽出した精製物等の総称を意味する。ここで、水蒸気蒸留は通常の通り、植物体又はその加工物に水蒸気を吹き込み、溜出分を冷却し水相と有機相に分け、有機相を取れば良く、又、抽出は、植物体又はその加工物に０．５～１０倍量の溶剤を加え室温であれば数

日、沸点付近の温度であれば数時間浸漬すればよい。溶媒としては、例えば、メタノールやエタノール等のアルコール類、酢酸エチルや蟻酸メチル等のエステル類、アセトニトリル等のニトリル類、ジエチルエーテルやテトラヒドロフラン等のエーテル類、クロロホルムや塩化メチレン等のハロゲン化炭化水素類、アセトンやメチルエチルケトン等のケトン類等が例示できる。本発明ではこれらの何れもが利用可能であるが、これらの内好ましいものは、蒸留などによって得た、植物体構成成分のうちの低沸点成分、即ち、沸点２００℃未満の成分である。これは、本発明の副腎皮質ホルモン分泌抑制剤が香気によって嗅覚を介して刺激する場合が最も効果的で安全な副腎皮質ホルモン分泌抑制作用を期待できるからである。本発明の副腎皮質ホルモン分泌抑制剤は後記実施例に示す如く、嗅覚を介して唾液中の副腎皮質ホルモンの濃度を下げる作用を有する。

【０００８】（２）ストレスの負荷と副腎皮質ホルモンの関係

ストレスと副腎皮質ホルモン、取り分け糖質コルチコイドの関係は深いとされているが、これらを実際に確かめた例はない。そこで、糖質コルチコイドとしてコルチゾールをとり、ストレスの負荷とコルチゾールの関係を知るために次のような実験を行った。即ち、被験者２０名を集め、２桁の加減乗除の計算を１題につき４秒の猶予で３０分間行わせ、その前後３０分に唾液を採取し、唾液中のコルチゾール濃度を後記発明の実施の形態に示すラジオイムノアッセイによって求めた。（（計算後のコルチゾールの濃度）－（計算前のコルチゾールの濃度））／（計算前のコルチゾールの濃度）＊１００の計算式より唾液中コルチゾールの増加率を求めた。同様に、それぞれ別の日に、猶予時間を３秒にした場合、問題を解く時間を４０分間にした場合のこの値も求めた。結果を表１に示す。この表よりストレスの負荷量に比例してコルチゾールの増加率も上昇することが判る。即ち、コルチゾールに代表される糖質コルチコイドの唾液中への分泌量が負荷されているストレスの強さの指標になることが判る。即ち、コルチゾールに代表される糖質コルチコイドの分泌量を下げる物質が、ストレスを緩和しうる物質であるといえる。

【０００９】

【表１】

条件	コルチゾールの平均増加率（%）
猶予4秒、３０分間	４３
猶予3秒、３０分間	６２
猶予4秒、４０分間	５６

【００１０】（３）本発明の副腎皮質ホルモン分泌抑制剤の作用

本発明の副腎皮質ホルモン分泌抑制剤は、香りとして嗅覚を刺激することにより、ストレスを緩和させる作用を有し、その結果として唾液中の副腎皮質ホルモンの分泌を抑制しその濃度を低下させる作用を有する。本発明の副腎皮質ホルモン分泌抑制剤が香りとして、その効果を発揮する用量は、０．０１～１０ｍｇ／m^3であり、この濃度で嗅覚を刺激するのが好ましい。本発明の基源植物は何れも食用に広く用いられているので、この様な濃度で毒性を発現する心配はない。

【００１１】（４）本発明の組成物

本発明の組成物は、上記副腎皮質ホルモン分泌抑制剤を含有することを特徴とする。組成物の種類としては、嗅覚を介して本発明の副腎皮質ホルモン分泌抑制剤による刺激を伝達しうるものであれば特段の限定はなく、例えば、ポプリ、ルームフレグランス、香水、化粧水等の香粧品、ガムやキャンディー等の食品、ジュースや清涼飲料水等の飲料等が好ましく例示できる。本発明の組成物では副腎皮質ホルモン分泌抑制剤以外に、これらの組成物で通常用いられている任意成分を自由に用いることが出来る。この様な任意成分としては、例えば、香粧品ではワセリンやマイクロクリスタリンワックス等のような炭化水素類、ホホバ油やゲイロウ等のエステル類、牛脂、オリーブ油等のトリグリセライド類、セタノール、オレイルアルコール等の高級アルコール類、ステアリン酸、オレイン酸等の脂肪酸、グリセリンや１，３－ブタンジオール等の多価アルコール類、非イオン界面活性剤、アニオン界面活性剤、カチオン界面活性剤、両性界面活性剤、エタノール、カーボポール等の増粘剤、防腐剤、紫外線吸収剤、抗酸化剤、色素、粉体類等が挙げられるし、食品や飲料では、矯味矯臭剤、甘味料、酸味料、油脂、増粘剤、乳化安定剤、水、炭酸、賦形剤、結合剤などが挙げられる。又、これら組成物における本発明の副腎皮質ホルモン分泌抑制剤の好ましい含有料であるが、香粧品では、０．０１～６０重量%が好ましく、０．０５～４０重量%がより好ましく、０．１～３０重量%が更に好ましい。食品或いは飲料では、０．０１～３０重量%が好ましく、０．０５～２０重量%がより好ましく、０．１～１０重量%が更に好ましい。これらの組成物は通常知られている方法により製造できる。

【００１２】

【発明の実施の形態】以下に例を挙げて本発明の実施の形態について詳細に説明するが、本発明がこれら例のみ

に限定を受けないことは言うまでもない。

【００１３】例１（製造例）

ラベンダーの乾燥全草１ｋｇを粉砕し、水蒸気蒸留にかけ水不溶分を集め、０．７ｇの副腎皮質ホルモン分泌抑制剤１を得た。

【００１４】例２（製造例）

ペパーミントの乾燥葉１ｋｇを粉砕し、水蒸気蒸留にかけ水不溶分を集め、１．１ｇの副腎皮質ホルモン分泌抑制剤２を得た。

【００１５】例３（製造例）

スペアミントの乾燥葉１ｋｇを粉砕し、水蒸気蒸留にかけ水不溶分を集め、０．８ｇの副腎皮質ホルモン分泌抑制剤３を得た。

【００１６】例４（製造例）

マージョラムの乾燥葉１ｋｇを粉砕し、水蒸気蒸留にかけ水不溶分を集め、０．７ｇの副腎皮質ホルモン分泌抑制剤４を得た。

【００１７】例５（製造例）

バジルの乾燥葉１ｋｇを粉砕し、水蒸気蒸留にかけ水不溶分を集め、１．２ｇの副腎皮質ホルモン分泌抑制剤５を得た。

【００１８】例６（製造例）

レモンバームの乾燥葉１ｋｇを粉砕し、水蒸気蒸留にかけ水不溶分を集め、０．９ｇの副腎皮質ホルモン分泌抑制剤６を得た。

【００１９】例７（製造例）

セイジの乾燥葉１ｋｇを粉砕し、水蒸気蒸留にかけ水不溶分を集め、０．８ｇの副腎皮質ホルモン分泌抑制剤７を得た。

【００２０】例８（製造例）

ローズマリーの乾燥葉１ｋｇを粉砕し、水蒸気蒸留にかけ水不溶分を集め、１．３ｇの副腎皮質ホルモン分泌抑制剤８を得た。

【００２１】例９（製造例）

キャットニップの乾燥葉１ｋｇを粉砕し、水蒸気蒸留にかけ水不溶分を集め、１．１ｇの副腎皮質ホルモン分泌抑制剤９を得た。

【００２２】例１０（製造例）

タイムの乾燥葉１ｋｇを粉砕し、水蒸気蒸留にかけ水不溶分を集め、０．６ｇの副腎皮質ホルモン分泌抑制剤１０を得た。

【００２３】例１１（製造例）

オレガノの乾燥葉１ｋｇを粉砕し、水蒸気蒸留にかけ水不溶分を集め、０．７ｇの副腎皮質ホルモン分泌抑制剤１１を得た。

【００２４】例１２（製造例）

紫蘇の乾燥葉１ｋｇを粉砕し、３ｌのメタノールで２時間還流し抽出し溶媒を溜去し、２．１ｇの副腎皮質ホルモン分泌抑制剤１２を得た。

【００２５】例１３（製造例）

ニホンハッカの乾燥葉１ｋｇを粉砕し、５ｌのメタノールで２時間還流し抽出して溶媒を溜去し、２．５ｇの副腎皮質ホルモン分泌抑制剤１３を得た。

【００２６】例１４～２０（配合例）

表２に示す処方でルームフレグランスを製造した。即ち処方成分を加熱溶解し、容器に流し込み固化させてルームフレグランスを得た。

【００２７】

【表２】

成分	例１４	例１５	例１６	例１７	例１８	例１９	例２０
ｶﾙﾅｳﾊﾞﾜｯｸｽ	５０	５０	５０	５０	５０	５０	５０
流動ﾊﾟﾗﾌｨﾝ	３０	３０	３０	３０	３０	３０	３０
例１	１０						
例２		１０					
例３			１０				
例４				１０			
例５					１０		
例６						１０	
例７							１０

【００２８】例２１～２７（配合例）

表３に示す処方でカーフレグランスを製造した。即ち処方成分を加熱溶解し、容器に詰め、芯を装着させてカームフレグランスを得た。

【００２９】

【表３】

成分	例21	例22	例23	例24	例25	例26	例27
エタノール	50	50	50	50	50	50	50
PEG400	30	30	30	30	30	30	30
例8	10						2
例9		10					2
例10			10				2
例11				10			2
例12					10		1
例13						10	1

【0030】例28～34

表4に示す処方で化粧水を作成した。即ち処方成分を80℃で加熱撹拌可溶化し冷却して化粧水を得た。

【0031】

【表4】

成分	例28	例29	例30	例31	例32	例33	例34
エタノール	10	10	10	10	10	10	10
プロパノール	5	5	5	5	5	5	5
ﾒﾁﾙﾊﾟﾗﾍﾞﾝ	0.1	0.1	0.1	0.1	0.1	0.1	0.1
水	82.9	82.9	82.9	82.9	82.9	82.9	82.9
例1	1						
例2		1					
例3			1				
例4				1			
例5					1		
例6						1	
例7							1

【0032】例35～41（配合例）

表5の処方に従ってヘアトニックを作成した。即ち、処方成分を秤込み、撹拌可溶化してヘアトニックを得た。

【表5】

成分	例35	例36	例37	例38	例39	例40	例41
エタノール	50	50	50	50	50	50	50
プロパノール	5	5	5	5	5	5	5
ﾄｳｶﾞﾗｼｼｷ	0.1	0.1	0.1	0.1	0.1	0.1	0.1
水	42.9	42.9	42.9	42.9	42.9	42.9	42.9
例8	1						0.2
例9		1					0.2
例10			1				0.2
例11				1			0.2
例12					1		0.1
例13						1	0.1

【0033】例42～48（配合例）

表6の処方に従ってキャンディーを作成した。即ち、処

方成分を１２０℃で加熱して一様にし、成型してキャンディーを得た。

【００３４】
【表６】

成分	例４２	例４３	例４４	例４５	例４６	例４７	例４８
白糖	５０	５０	５０	５０	５０	５０	５０
水飴	３０	３０	３０	３０	３０	３０	３０
クエン酸	５	５	５	５	５	５	５
例１	１５						
例２		１５					
例３			１５				
例４				１５			
例５					１５		
例６						１５	
例７							１５

【００３５】
【実施例】
実施例１
例１～例１３の副腎皮質ホルモン分泌抑制剤１～１３について、副腎皮質ホルモン分泌抑制作用を調べた。被験者２０名に対し、副腎皮質ホルモン分泌抑制剤１～１３の存在下、前述の猶予４秒、３０分間の計算負荷作業を行わせた。コントロール群は香りの存在無しで行った。この作業の前後に唾液を採取し、ガンマー・コートコーチゾンを用いてコルチゾールの定量を行った。即ち、唾液を－２０℃、２４時間で凍結させ、５℃に戻し３０００ｃｐｍ、１５分で遠心分離し上清を取った。この上清を測定直前まで－２０℃で保存した。キットのトレーサー液１バイアルをキットの緩衝液１００ｍｌと良く混和させトレーサー緩衝液とした。キットの抗体チューブそれぞれに検体、ブランクとして生理食塩水、コルチゾールの標準液を２００μｌづつ入れた。これらのチューブそれぞれにトレーサー緩衝液１ｍｌを加えた。トータルカウント測定用チューブ（Ｔ１，Ｔ２）にトレーサー緩衝液を１ｍｌづつ加えキャップをしてトータルカウントチューブとした。これらのチューブを３７℃、４５分インキュベートした。内容液を除去し、ガンマーカウンターで全てのチューブの放射能を測定した。このうち標準液に対する放射活性をプロットし、検量線を作成し、この検量線より各検体中のコルチゾールの濃度を算出した。尚、比較品としては、森林の香気成分である青葉アルコールと柑橘類に含まれる香気成分であるリナロールを用いた。結果を表７に示す。表の数値の単位はμｇ／ｄｌである。この表より本発明の副腎皮質ホルモン分泌抑制剤は有意に唾液中のコルチゾールの濃度を低下させていた。又、青葉アルコールやリナロールに比較しても低下の度合いは高かった。又、この実験結果が定量的にハーブの抗ストレス効果を評価していることも明かである。

【００３６】
【表７】

検体	作業前	作業後
コントロール	０．２４０	０．３５１
副腎皮質ホルモン分泌抑制剤１	０．２４７	０．３１２
副腎皮質ホルモン分泌抑制剤２	０．２４３	０．２９９
副腎皮質ホルモン分泌抑制剤３	０．２５０	０．２９４
副腎皮質ホルモン分泌抑制剤４	０．２３９	０．２８７
副腎皮質ホルモン分泌抑制剤５	０．２５１	０．３３１
副腎皮質ホルモン分泌抑制剤６	０．２４６	０．３１９
副腎皮質ホルモン分泌抑制剤７	０．２５５	０．３３５
副腎皮質ホルモン分泌抑制剤８	０．２４１	０．３２２
副腎皮質ホルモン分泌抑制剤９	０．２４９	０．３２９
副腎皮質ホルモン分泌抑制剤１０	０．２５３	０．３４１
副腎皮質ホルモン分泌抑制剤１１	０．２３５	０．３３３
副腎皮質ホルモン分泌抑制剤１２	０．２４５	０．３２８
副腎皮質ホルモン分泌抑制剤１３	０．２５５	０．３３０
青葉アルコール	０．２５６	０．３４５
リナロール	０．２４０	０．３３９

【００３７】
【発明の効果】本発明によれば、手軽にストレスの指標である、副腎皮質ホルモンの分泌を抑制し、体液中の副腎皮質ホルモンの濃度を低下させることが出来る。